IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al.		
Application No.: 10/646,436		
Filed: 8/21/2003	Group Art Unit:	1635
Title: RNAi Probes Targeting Cancer-Related Proteins	Examiner:	Kimberly Chong
Attorney Docket No.: UBC.P-030		

REPLY BRIEF FOR APPELLANT

This Reply Brief is filed in support of Applicants' Appeal from the final rejection mailed 2/19/2010 and in response to the Examiner's Answer mailed August 2, 2010.

On Page 5 of the Examiner's Answer the argument is made that:

> one of ordinary skill in the art would have been expected to be able to design an siRNA targeted to the same region as the claimed RNA sequence because Tuschl et al. details the steps to effectively find a target site in any RNA and design and test siRNA for specific RNAi activity.

It is pointed out that the Examiner has not shown that applying any of the teachings of Tuschl would result in Seq ID no. 10.

The Examiner continues by stating that:

> Miyake et al identifies an optimal target region, region of TRPM-2 gene that is targeted by the claimed SEQ ID No: 10, one of ordinary skill in the art would have expected to make the claimed RNA molecule comprising SEQ ID NO. 10.

It would be more correct to say that Miyake et al. disclose a target site **for antisense DNA** inhibition. Thus, this argument reflects the continuing assumption that one skilled in the art would expect an antisense DNA target to be of use as an siRNA target. However, the art of record shows that the standards for selecting targets for dsRNA molecules are completely different from the standards for selecting antisense candidates.

It is noted in the response to Applicants arguments, on Page 11 of the Examiner's Answer, the Examiner acknowledges the argument made by Applicants and then states that it is not persuasive. It is stated that Miyake et al provide motivation "to reduce expression of the gene (TRPM-2) **and to target the translation initiation site.**" The Miyake et al. reference only makes the latter suggestion, however, with respect to DNA antisense, not an RNAi molecule. The Examiner has not stated why a person skilled in the art would extend this suggestion to an RNAi molecule and indeed cites to Tuschl, Holen, Fosnaugh and Hammond for the superiority of RNAi over antisense but not for any teaching of relevance to use of **this** antisense (the Miyake et al) as a basis for selecting an RNAi target.

The closest the cited art comes to addressing this issue is in example 2 of Fosnaugh, ¶ 232, where antisense targets are mentioned as one type of target to be considered among numerous others. Fosnaugh then teaches that "various parameters can be used to determine which sites are the most suitable target sites within the target RNA sequence." Thus, just being an antisense target is not enough to provide an expectation of success as an RNAi target. Applying Fosnaugh's standards for selection (as set forth in Example 3 of the reference) would not result in selection of the Miyake et al target as a suitable target for RNAi.

Finally, the Examiner states (Page 5) that

> because Holen et al demonstrates the routine nature of designing siRNA sequence that target a gene every 3 nucleotides, one of ordinary skill in the art would have designed an RNA molecule targeted to TRPM-2 as taught by Miyake et al.

Miyake does not teach an RNA molecule targeted to TRPM-2. Furthermore, to the extent this statement is otherwise understood, it appears that the Examiner is arguing that because the methods for finding the specific sequence now claimed are known, the sequence is obvious. This

directly contradicts the language of 35 USC § 103(a) which provides that the manner in which the invention was made shall not negative patentability.

Respectfully submitted,

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